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EXAMINER

HILL, KEVIN KAI

ART UNIT	PAPER NUMBER
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1633

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/578,402	Applicant(s) GLIMCHER ET AL.	
	Examiner KEVIN K. HILL	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 February 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4,5,8-17 and 55-67 is/are pending in the application.
- 4a) Of the above claim(s) 4,5,8-10,12,14,15,56,59,60,62-65 and 67 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,11,13,16,17,55,57,58,61 and 66 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Detailed Action

Election/Restrictions

Applicant's response to the Requirement for Restriction, filed on July 22, 2009 is acknowledged.

Applicant has elected the invention of Group I, Claims 2-5 and 11-17, drawn to a method for identifying a compound which modulates an interaction between a first and a second polypeptide, the method comprising contacting *in vitro* a non-transgenic cell having a first polypeptide comprising a binding portion of a KRC polypeptide and a second polypeptide comprising a binding portion of a polypeptide selected from the group consisting of GATA3, SMAD or Runx2, classified in class 435, subclass 4.

Within Group I, Applicant has elected the following species, wherein:

- i) Claims 1 and 22 are generic to the host cell is a mouse T cell;
- ii) determination method steps from the lists recited in claims 9-11 and 13-15, is co-immunoprecipitation (Claim 11);
- iii) second polypeptide indicator recited in Claims 1, 4-5 and 22 is GATA3; and
- iv) biological activity species that is to be measured from the list recited in Claims 13, 19 and 21 is Th2 cell differentiation.

Amendments

In the reply filed February 4, 2010, Applicant has cancelled Claims 2-3, 6-7 and 18-54, withdrawn Claims 4-5, 8-10, 12, 14-15, 59-60, 62-65 and 67, and amended Claims 11 and 16-17.

Claims 4-5, 8-10, 12, 14-15, 56, 59-60, 62-65 and 67 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

This application contains claims drawn to an invention nonelected with traverse in the reply filed on July 22, 2009. Applicant is reminded that the restriction/election requirement was made final in the Office Action of October 7, 2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP §821.01.

Claims 1, 11, 13, 16-17, 55, 57-58, 61 and 66 are under consideration.

Priority

This application is a 371 of PCT/US04/36641 filed November 3, 2004, which is a continuation of U.S. application 10/701,401 filed November 3, 2003, which is a continuation-in-

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part of PCT/US02/14166 filed May 3, 2002. Applicant's claim for the benefit of a prior-filed application parent provisional application 60/288,369 filed May 3, 2001 under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Examiner's Note

Unless otherwise indicated, previous objections/rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the February 4, 2010 response will be addressed to the extent that they apply to current rejection(s).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

1. **The reply filed on February 4, 2010 is not fully responsive** to the prior Office Action because of the following omission(s) or matter(s):

The amendments to the claims do not comply with the Revised Amendment Practice of 37 CFR 1.121 (See OG Notice 23 September 2003). Specifically, Claims 11 and 16-17 are annotated as being "Currently Amended"; however, Applicant provides no markings to indicate that changes that have been made relative to the immediately prior version of the claims.

§1.121 Manner of making amendments in applications.

(c) Claims. Amendments to a claim must be made by rewriting the entire claim with all changes (e.g., additions and deletions) as indicated in this subsection, except when the claim is being canceled. Each amendment document that includes a change to an existing claim, cancellation of an existing claim or addition of a new claim, must include a complete listing of all claims ever presented, including the text of all pending and withdrawn claims, in the application. The claim listing, including the text of the claims, in the amendment document will serve to replace all prior versions of the claims, in the application. In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered).

(2) When claim text with markings is required. All claims being currently amended in an amendment paper shall be presented in the claim listing, indicate a status of "currently

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amended," and be submitted with markings to indicate the changes that have been made relative to the immediate prior version of the claims. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived. Only claims having the status of "currently amended," or "withdrawn" if also being amended, shall include markings. If a withdrawn claim is currently amended, its status in the claim listing may be identified as "withdrawn- currently amended."

Claim Rejections - 35 USC § 112

2. **Claims 1, 11, 13, 16-17, 55, 57-58, 61 and 66 stand rejected under 35 U.S.C. 112, first paragraph**, because the specification, while being enabling for non-transgenic human indicator cells, does not reasonably provide enablement for an enormous genus of indicator cell types such as prokaryotic, fungal, plant, invertebrate, vertebrate, avian or mammalian cells that endogenously encode GATA3 and a human KRC polypeptide having the amino acid sequence of SEQ ID NO:2.

Response to Arguments

Applicant argues that claim 1 links multiple species of indicator cells, e.g., which endogenously express the molecules which have been found to interact as well as which express exogenous forms of these molecules. Applicants note that one of ordinary skill in the art armed with the teachings of the instant specification could perform the claimed methods without undue experimentation. While Applicants understand that the Examiner is currently considering the species of mouse cells, it is Applicants understanding that this is for search purposes only.

Applicant's argument(s) has been fully considered, but is not persuasive. All questions of enablement are evaluated against the claimed subject matter. The focus of the examination inquiry is whether everything within the scope of the claim is enabled. As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. >*AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244, 68 USPQ2d 1280, 1287 (Fed. Cir. 2003);< *In re Moore*, 439 F.2d 1232, 1236, 169 USPQ 236, 239 (CCPA

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1971). MPEP §2164.08. In the instant case, the claims are enormously broad for reasonably embracing an enormous genus of prokaryotic, fungal, plant, invertebrate and vertebrate cell types [0125]. However, the instantly elected invention is to the use of a non-transgenic cell, and thus each of the first and second polypeptides must necessarily be naturally encoded by the genomes of the indicator cell. Neither the claims nor the specification provide enabling support for the enormously broad genus of cultured non-transgenic cell types.

Claim Rejections - 35 USC § 103

3. **Claims 1, 11, 16-17, 55, 57-58 and 66 stand rejected under 35 U.S.C. 103(a)** as being unpatentable over Emerson (U.S. 2002/0022021; of record) in view of Haenlin et al (1997; of record), Matthews et al (2000; of record), Cubbada et al (1997; of record), (1995; of record in IDS), Wu et al (1996; of record in IDS), Hicar et al (2001; of record in IDS) and Ting et al (1996; of record).

Response to Arguments

Applicant argues that they were the first to discover the interaction of KRC with GATA-3 and submit that, given the knowledge in the art, it could not have been predicted at the time of filing that KRC would bind to GATA- 1, let alone to GATA-3. Absent this predictability, the skilled artisan would have had no motivation whatsoever to modify the cited references to arrive at the claimed methods.

Applicant's argument(s) has been fully considered, but is not persuasive. Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). See MPEP §2143.02. In the instant case, a) the prior art within the same field of endeavor as that of Applicant's invention taught a similar or analogous method to assay a first polypeptide and a second polypeptide comprising a GATA polypeptide in a method for identifying a compound which modulates an interaction between a first polypeptide and a second polypeptide (Emerson), b) there were design incentives which would have prompted adaptation of the known method, specifically the recognition of a protein-protein interaction between a GATA factor and a polypeptide comprising a CCHC motif, such as KRC (Haenlin et al, Matthews et al, Cubbada et al, Wu et al, Hicar et al), c) the differences between the claimed invention and the prior art were

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encompassed in known variations or in a principle known in the prior art, specifically the routinely practiced assaying of physical interactions between a first polypeptide of interest and second polypeptide of interest by those of ordinary skill in the art pursuing known options within his or her technical grasp (Emerson, Haenlin et al), d) those of ordinary skill in the art in view of the design incentives could have implemented the claimed variation of the prior art, and the claimed variation would have been predictable, specifically in light of the topology of CCHC zinc-fingers, present in KRC and essential for GATA-binding (Matthews et al, Cubbada et al, Hicar et al), and e) GATA-3 was recognized in the prior art to be expressed in the same cell type as KRC, specifically T cells and T lymphocytes (Wu et al, Hicar et al, Ting et al).

Applicant argues that the assumption that all CCHC zinc fingers bind to all GATA-1 family transcription factors is incorrect. It was well known in the art at the time of filing that only a subset of CCHC zinc fingers bind to GATA-1 proteins (Figure 1, Liew et al, Appendix A). Only three of the five CCHC zinc fingers in *Drosophila* Ush actually bind to the *Drosophila* GATA-1 homologue, Pannier. Accordingly, it could not have been predicted, at the time of filing, whether a particular CCHC would bind to GATA-1. At the time of filing, it was well known in the art that only one of the two Ush CCHC fingers disclosed in Figure 6 actually binds to *Drosophila* GATA-1 homologue. Thus, from the available data it could not have been predicted whether a Shn CCHC zinc finger will bind to the *Drosophila* GATA-1 homologue, let alone whether KRC will bind to GATA-3.

Applicant's argument(s) has been fully considered, but is not persuasive.

As a first matter, arguments of counsel cannot take the place of **factually supported objective evidence** in the record. See *In re Schulze*, 346 F.2d 500, 602, 145 USPQ 716, 718 (CCPA 1965), *In re Huang*, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). The Examiner is unable to find a copy of Liew et al in the papers filed February 4, 2010. It appears the Appendix A was not submitted.

As a second matter, "Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness." *In re Rinehart*, 531 F.2d

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1048, 189 USPQ 143 (CCPA 1976). See MPEP §2143.02. In the instant case, the substantive issue is that the ordinary artisan at the time of the invention recognized that proteins containing CCHC zinc fingers are capable of binding to GATA factors. That three of the five CCHC zinc fingers within Ush actually bind to GATA clearly evidences that the ordinary artisan possessed a reasonable expectation of success [60%, more likely than not] that a CCHC domain will bind to a GATA factor given the structural homology of the CCHC domain.

Haenlin et al taught the physical interaction between a GATA-1-like factor, Pannier, and a zinc-finger protein, Ush. Matthews et al taught that the topology of CCHC zinc-fingers, present in Ush, is essential for GATA-binding. Thus, based upon the structural homologies between CCHC zinc-finger domains and the structural homologies between GATA factors, at the time of the instantly asserted invention, the ordinary artisan possessed a reasonable expectation of success for a first protein having a CCHC zinc-finger domain to bind to a GATA factor.

KRC polypeptides comprising a CCHC zinc finger motif were known in the prior art (Cubbada et al, Wu et al, Hicar et al). Ting et al taught that GATA-3 is expressed in the same cells as KRC.

"A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton." *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1397 (2007). "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *Id.* Office personnel may also take into account "the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at ___, 82 USPQ2d at 1396.

Thus, it is the Examiner's position that the ordinary artisan, in light of the structural homologies between CCHC zinc-finger domains and between GATA factors, that the topology of CCHC zinc-fingers is essential for GATA-binding, and the knowledge generally available in the art at the time of the invention, the ordinary artisan possessed a reasonable expectation of success for a first polypeptide comprising a KRC polypeptide to bind a second polypeptide comprising a GATA3 polypeptide.

Applicant argues that the Examiner has provided no evidence whatsoever to suggest that the binding of CCHC zinc fingers to GATA-3 could have been predicted from the prior art.

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Moreover, that at the time of filing it was well known in the art that GATA-1 and GATA-3 were sufficiently functionally different such that GATA-3 could not substitute for GATA-1 in GATA-1 null mice (see Tsai et al., submitted herewith as Appendix B). Applicants submit that these functional differences between GATA-1 and GATA-3 preclude any predictability that GATA-1 and GATA-3 would bind to the same molecules in the cell. Indeed, these functional differences could easily be due to the inability of GATA-3 to bind to CCHC zinc finger proteins.

Applicant's argument(s) has been fully considered, but is not persuasive.

As a first matter, arguments of counsel cannot take the place of **factually supported objective evidence** in the record. See *In re Schulze*, 346 F.2d 500, 602, 145 USPQ 716, 718 (CCPA 1965), *In re Huang*, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). The Examiner is unable to find a copy of Tsai et al in the papers filed February 4, 2010. It appears the Appendix B was not submitted.

As a second matter, arguments of counsel cannot take the place of **factually supported objective evidence** in the record. See *In re Schulze*, 346 F.2d 500, 602, 145 USPQ 716, 718 (CCPA 1965), *In re Huang*, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). Attorney statements regarding, e.g. inoperability of the prior art, are not evidence without a supporting declaration. Applicant has provided no evidence establishing a nexus between the domain mediating an interaction between CCHC zinc-fingers and GATA proteins and the functional differences between GATA-1 and GATA-3 transcription factors such that the different functions between GATA-1 and GATA-3 are necessarily, solely and absolutely due to the domain mediating an interaction between CCHC zinc-fingers and GATA proteins.

The substantive issue is that the ordinary artisan at the time of the invention recognized that proteins containing CCHC zinc fingers are capable of binding to GATA factors (Haenline et al, Matthews et al). The topology of CCHC zinc-fingers is essential for GATA-binding. Thus, based upon the structural homologies between CCHC zinc-finger domains and the structural homologies between GATA factors, at the time of the instantly asserted invention, the ordinary artisan possessed a reasonable expectation of success for a first protein having a CCHC zinc-finger domain to bind to a GATA factor.

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KRC polypeptides comprising a CCHC zinc finger motif were known in the prior art (Cubbada et al, Wu et al, Hicar et al). Ting et al taught that GATA-3 is expressed in the same cells as KRC.

"A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton." *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1397 (2007). "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *Id.* Office personnel may also take into account "the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at ___, 82 USPQ2d at 1396.

Thus, it is the Examiner's position that the ordinary artisan, in light of the structural homologies between CCHC zinc-finger domains and between GATA factors, that the topology of CCHC zinc-fingers is essential for GATA-binding, that the CCHC zinc-finger containing protein KRC is expressed in the same cell as GATA-3, and the knowledge generally available in the art at the time of the invention, the ordinary artisan possessed a reasonable expectation of success for a first polypeptide comprising a KRC polypeptide to bind a second polypeptide comprising a GATA3 polypeptide.

4. **Claims 13 and 61 stand rejected under 35 U.S.C. 103(a)** as being unpatentable over Emerson (U.S. 2002/0022021; of record) in view of Haenlin et al (1997; of record), Matthews et al (2000; of record), Cubbada et al (1997; of record), (1995; of record in IDS), Wu et al (1996; of record in IDS), Hicar et al (2001; of record in IDS) and Ting et al (1996; of record), as applied to Claims 1, 11, 16-17, 55, 57-58 and 66 above, and in further view of Lee et al (1998; of record).

Response to Arguments

Applicant does not contest the teachings of Lee et al as applied to the obviousness to substitute a first endogenous reporter gene as taught by Emerson with a second endogenous reporter gene, more specifically the Th2 cytokine gene IL-5 as taught by Lee et al in a method for identifying a compound which modulates an interaction between a first polypeptide and a second polypeptide comprising determining the effect of the test compound identified as modulating the interaction between the first and second polypeptide on Th2 cytokine production with a reasonable expectation of success because the simple substitution of one known element

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for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Conclusion

5. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KEVIN K. HILL whose telephone number is (571)272-8036. The examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill/
Examiner, Art Unit 1633